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09/918,601	07/30/2001	Garry P. Nolan	A-64260-5/DJB/RMS/AMS	6631

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/918,601	Applicant(s) NOLAN, GARRY P.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/27/03, 5/16/03* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-26,28-30,32,34-37,40-52 and 54-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-26, 28-30, 32, 34-37, 40-52 and 54-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Claims

Claims 1-22 have been cancelled in the amendment of 7/30/01. Claims 23-58 have been added.

Claims 27, 31, 33, 38-39, 53 and 58 have been cancelled in the present Amendment, 12/23/02.

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are pending and under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 47-52 and 54-57 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter and lacks patentable utility for reasons advanced in the last Office action.

Response to Arguments

Applicant argues that the used and sale of libraries of compounds is well known in the biological and chemical arts. The development of libraries having novel features is important in the field of molecular biology. Applicant attached an offer for sale of a retroviral cDNA expression library. It is argued that one of skill in the art would appreciate the commercial value of

such libraries, and their utility in the molecular biology workplace. The Patent Office has recognized the utility and commercial value of libraries of agents, and may(sic) such libraries have been patented. In reply, applicant has not argued the specific or practical utility of the library except for its commercial value. However, the commercial value of a compound does not have any bearing as to whether a compound (library, in the instant case) has a utility or not. All compound products have commercial value but not all commercially valuable products have the utility as required by the statute. As for other patented library as having been granted by the Office, it is settled law, that each case is treated on its own merit.

Applicants argue that the instant library provides a means of screening for randomized bioactive agents and is specifically useful in the methods of the invention. In reply, as clearly pointed out by applicants the library is only a means by which a useful bioactive agents can be identified. All products, naturally or non-naturally occurring undergo screening. But the source of the product, whether natural resources or synthetic as the instant library, in of itself, does not have a patentable utility. No specific utility can be attributed to a collection of compounds as libraries as the components therein are undefined or unknown. Only after screening said library can a

specific product with a specific utility can be obtained therefrom. However, a library per se, as admitted by applicants, is only useful in a method of screening a product contained therein. The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a library of as yet undetermined structure, function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the library as of the filing date is useful. Except to screen for a compound, which ultimately is the one that has the specific utility. Until some

actual and specific significance can be attributed to the library an artisan would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

"Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696. In *Brenner*, the Court approved a rejection for failure to disclose any utility for a compound where the compound was undergoing screening for possible compounds the utility of which has also not been identified. *Brenner*, 148 USPQ at 690. Here, there is no evidence that the claimed isolated compounds have any utility. *See In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) (quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the

compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.') .

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A). The as-filed specification does not describe a method by which a cell can be ***in vitro*** screen using the recited step. It is not clear how a cell can be screen in vitro. The as-filed specification describes, appropriately so, an **in vitro** screening of bioactive molecules that cause phenotypic changes to a cell.

Claims 23-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific library as provided in Figs. 1 and 2 (Example 2), a tumor cell and other specific embodiments disclosed in the

specification does not reasonably provide enablement for the broadly claimed variables encompassed by the claimed method and library for reasons set forth in the last Office action.

Applicant argues that practice of the claimed invention would not require undue experimentation by one of skill in the art. In order to practice the invention, one of skill in the art needs to know the parameters for several aspects of the claimed method. Coding sequence and vector selection and transfection of the vector into appropriate cells are required to practice the invention. Guidance of the practice of these steps is disclosed in the subject application. Applicant however admits that it is well known in the art that **protein expression is dependent on the host cell, expression vector, regulatory elements,** etc. Applicant further admits that the literature provides ample guidance for selecting the **appropriate combination of elements and vectors**. In reply, as admitted by applicants the literature discloses selection of appropriate combination of elements and not any elements as generically claim. The teachings in the literature are specific for specific combinations of elements. As further admitted by applicant, protein expression is dependent on host cell. That is, the host cell will express only components that do not deleteriously affect its function or expression. Or will express the components in a library that

would be representative of the compounds therein. The claims as broadly written, does not take this into account.

Applicant argues that the recitation in a claim of a generic element for example promoters, retrovirus does not require that the specification list each and every promoter that might be used with the invention. Rather, one may rely on the thousand of promoters known in the art to be useful in initiation transcription of a proximal gene. In reply, the claims do not recite for any promoters. Furthermore, applicant is not required to list every conceivable promoter or retroviruses. Rather, a reasonable assurance that the single enabled or example provided in the specification sufficiently enables the broad scope of the claims.

Applicant argues that a patent need not teach and preferably omits what is well known in the art. However, as apparent from applicant's arguments, it appears that everything is well known in the art. Resulting in omitting the essential or particular components require for the successful accomplishment of the invention. It is further argued that the law does not require that every detail of the working examples be reiterated as a limitation in the claims. In reply, it would appear that the working examples that have been provided have been actually done by applicant. Rather than the generalized statement in the

specification. The specification does not teach the applicability of the different components e.g., libraries of defined sequences to the instant library of unknown components or reaction to any type of cells. In a highly undeveloped and unexplored art as gene technology, examples direct a skilled artisan as to the applicability of the broad generic claims to any library of undefined components or to any type of cells that come in contact with the library.

As stated in the last Office action, there are too numerous factors to determine for the successful practice of the claimed invention. A priori statement as to the applicability of a specifically defined factor, to date, has not been made to broad claims as the instant claims.

[As suggested in the last Office action, this rejection can be obviated by reciting method steps as disclosed in Figs. 1 and 2 with the specific biased random library of nucleic acid and tumor cells].

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons as stated in the last Office action.

Response to Arguments

A). Applicant argues that the term "minimize" is provided in the present application. It means minimizing stop codons in the randomized portion. To alleviate the problem of stop codons interfering with peptide synthesis, random residues are encoded as NNK. This allows for encoding of all **potential** amino acids but importantly preventing the encoding of two stop residues TAA and TGA. Thus, libraries encoding a 10 amino acid peptide will have a 15.6% chance to terminate prematurely. In response, applicant cannot read limitations in the specification into the claim. It appears from applicant's argument that the NNK is essential for the minimizing or preventing of encoding two stop residues.

Applicant argues that the metes and bounds of the claimed "phenotype", "cell", "transdominant intracellular bioactive agent", "molecular library of biased randomized nucleic acids", and "class of molecules" are defined in the specification. They

include, but not limited for the phenotypic changes; gross physical changes such as cell morphology, cell growth, viability adhesion and other changes. In reply, the long list provided by applicant appears not to be limited thereto but still include others not given in the list. It is apparent that the claim has not been circumscribed with particularity.

B). Applicant argues that the identification of a bioactive peptide as set forth in claims 23 and 24, need not comprise an isolation step. In reply, newly amended claims 23 and 24 do not recite for isolation of the bioactive agent rather of the cell. Applicant further argues that many schemes are known in the art in which one identify a sequence through position, not through isolation. In response, the specification or claims do not recite for the positioning identification, except isolating step. It is further argued that the steps recited in claims 25 and 26 are not inherently part of the base claim and do provide a limitation of the base claim. In reply, it is not clear as to the purpose of only screening cells without isolating and identifying the cell. Thus, in order that the cell can be determined for any phenotype changes, isolation is required.

C). The rejection no longer applies with the cancellation of claim 27.

D). The rejection is no longer applicable with the amendment to claim 29.

E). It is argued that group of molecules comprising sequences both with and without a fusion partner is clearly generic to the subgroup comprising sequences with a fusion partner. In reply, as applicants state different groups of molecules comprised a fusion partner. Applicants have not responded to the following rejections: the metes and bounds of the claimed "presentation sequence" and "conformationally restricted **form**". The term "capable" connotes uncertainty as to whether, in fact, said presentation of the product occurs in a conformationally restricted form. Since applicant has not responded to these rejections, it is believed that applicant is acquiescing therewith. Claim 30.

F). In view of the amendments to claims 33-37, the rejection no longer applies.

G). Claims 40-46 broadens the base claim. The base claim does not recite a conjugate for the n.a. or the encoded bioactive agent. The metes and bounds of these sequences are indefinite. These sequences as recited in claims 40-46 are different in structures, kind and/or length or other characterizing features. Since applicant has not responded to

this rejection, it is believed that applicants are acquiescing therewith.

I). See the response above for claims 54-56, under paragraph E. The base claim does not recite for a fusion partner.

J). Claim 58 rejection is withdrawn with the cancellation of the claim.

The newly amended claims are rejected as follows:

1. Claims 23 and 24 are unclear as to the step of in vitro screening for a cell as recited in the preamble. The body of the claim does not recite for an **in vitro** screening. It is not clear how this is done for a cell.

2. Claim 26 broadens the base claim as to the identifying step of the candidate bioactive peptide. It is not clear as to what constitute a candidate bioactive peptide, in the context of the claim.

3. The metes and bounds of the class of molecules recited in claim 29 are not clearly circumscribed by claim 29.

Double Patenting

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are rejected under the judicially created doctrine of obviousness-

type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,365,344('344 Patent) for reasons of record.

Claims 23-26, 28-30, 32, 34-37, 40-52 and 54-57 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 23-38 of copending Application No. 09/727,715('715 application) or 09/916,940 or 08/963,368 or 08/787,738.

Response to Arguments

Applicant argues collectively the obviousness double patenting rejection for the issued Patent and copending applications. Applicant urges that one of skill in the art, upon reading the claims of the above-cited applications and patents would not reasonably expect to be able to produce or use a library comprising a randomized sequence biased to minimize stop codons and a randomized sequence biased to interact with a class of molecules. Such features are not obvious variation of the cited claims. There is no suggestion of such a library. In reply, one having ordinary skill in the art would obviously know that each of the random library contains a stop codon. Applicant states above, to alleviate the problem of stop codons interfering with peptide synthesis, random residues are encoded as NNK. This allows for encoding of all **potential** amino acids but importantly preventing the encoding of two stop residues TAA

and TGA. Thus, libraries encoding a 10 amino acid peptide will have a 15.6% chance to terminate prematurely. In response, applicant cannot read limitations in the specification into the claim. Furthermore, each of the copending applications and issued patents discloses said random library with biased stop codon. There is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will

expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-7924.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1627

tdw

7/24/03